Outcompeting Land Grabbing by bio-based Products using a novel Approach

A Human Practices Report for the SYNENERGENE Project

Handed in on October 14, 2016 by the 2016 Marburg iGEM Team:

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Abbreviations

FAO – Food and Agriculture Organization of the United Nations

GMO – Genetically modified organism

ha – Hectares

NGO – Non-Governmental Organisation

PEG - Polyethylenglycol

Acknowledgements

We kindly like to thank the Rathenau Institute for their intellectual and financial support of the 2016 Marburg iGEM team. Their help greatly facilitated our work on artificial endosymbiosis and its possible implications.

We would also like to thank our advisors Tarryn Miller and Daniel Hürtgen for helping us so much with the struggles in the lab on a daily basis.

Additionally, we'd like to acknowledge our advisors Dr. Tobias Erb and Dr. Gert Bange and their lab teams for providing us with intellectual input, lab space and consumables for our laboratory work during this project.

Furthermore, we would like to thank Max Mundt, Anne Löchner and Nicolas Krink for his help during the early stages of the project.

Summary

The occurrence of large scale land acquisitions in third world countries, commonly called "land grabbing" in media reports, has gained much attention throughout the past years. We find that underlying megatrends for these land deals are driven by rising world population and thereby increasing food demand, which is even increased by a nutrition transition towards a more animal product based consumption. Additional future food supply can be provided through yield increases and increasingly costly area expansion. The competition between Biofuel and food production puts pressure on international food prices and played a role in the 2008 food price spikes. This period of high and volatile food prices have raised concerns about food security in net food importing nations. Some importing countries sought to ensure supply, thereafter, through land grabs which concentrate on developing countries and foremost in Sub-Saharan Africa. Here, yield gaps are biggest on a global scale and weak customary land right protection is frequent. Investors see biofuel production as a lucrative investment and thus the majority of investment projects either target biofuel production or outputs with flexible use for biofuels and human consumption. The rise of land acquisition is seen as a threat to indigenous populations in the target countries with negative outcomes like dispossession and enclosure of commons upon which their livelihoods depend on.

Our lab project aimed to establish an artificial endosymbiosis between two organisms *Saccheromyces cervisiae* (yeast) and *Escherichia coli*, in order to enhance the production of bioproducts . As a proof of concept, our system was engineered to produce perillyl alcohol, which can be used as a precursor for biofuel production and medically valuable compounds. The advantage of using artificial endosymbiosis is that it can increase efficiency in product output. In this system, *E. coli* is modified so that it produces limonene which is transformed into perillyl alcohol by the symbiotic yeast. Dependency between both organisms, is crucial for establishing an endosymbiosis. This is achieved through a malonate exchange. The fused organisms still need a carbon source in form of sugar, such as glucose or sucrose. In order to mitigate the use of plant matter from the grabbed land for biofuels, the linkage of another organism (a photosynthetically active cyanobacterium) to the symbiont is needed to establish a system which no longer relies on farmland inputs. Our production facilities will require light as their sole energy source with minimum other inputs, however, will require high initial capital investments in order to begin production. Future research may make use of existing infrastructure, while production facilities are likely to be built in favourable environments, which are characterised by public acceptance and lower regulatory burdens.

This system would make use of natural light sources, which is a renewable and sustainable source of energy. Therefore, regions with high radiation are favoured. These regions could be found in Sub-Saharan Africa and therefore represent a chance for offsetting land grabbing in the regions that are most severely affected by it. In doing so, we hope to lift pressure from agricultural markets and thereby limit dispossession and enclosure of commons, which is severely harmful to indigenous people.

Introduction

"Outsourcing's third wave", "land rush" and "a form of neo-colonialism". These are terms that have been used in media reports over the past eight years for the phenomenon of land grabbing. Large scale land acquisitions of foreign investors in land abundant countries have seen a tremendous increase since 2008 (The Economist, 2009).

Therefore, we try to assess the problems surrounding large scale land deals and present our biotechnological approach to tackle them. This report is structured into two parts: The first, is dealing with an "Application Scenario" which covers the occurrence of land grabbing and how our idea could tackle it. In the beginning of the following section (section 1), this report aims to outline the underlying megatrends in world population. We will further shed light on the future development of international food demand and the nutrition transition happening in many developing countries. Thereafter, trends in agricultural supply and commodity prices will be explained, as they represent some driving forces in the complexity of land grabbing.

Section 2 of this report will give a definition of land grabbing and examine the underlying trends and patterns. One major factor is biofuel production, thus we will highlight the role that biofuels play in the rise of large scale land acquisitions. Furthermore, we present evidence why the occurrence of large scale land acquisition have raised concerns among scientists and Non-Governmental Organisations (NGOs), which demonstrate their alarm through drastic words sent out through publications and media releases.

As Synenergene aims to promote *responsible research and innovation*, we present our research project, which tries to tackle land grabbing by artificial endosymbiosis, in section 3. This report aims to show that there is the possibility to generate multi-purpose outputs through production in bioreactors. These outputs can be utilised in biofuel production and thereby lift pressure on international land markets generated by biofuel demand.

In section 4, we draw a conclusion on our findings based on the results obtained in the synthetic endosymbiosis project. We outline, how we one could imagine an application of the obtained results. We focus on the implications that a successful establishment of artificial endosymbiosis can have on the areas affected the hardest by land grabbing.

The second part of this report tries to give two "Techno-Moral Scenarios" which also draw on the findings from the artificial endosymbiosis project. We try to show what a possible

adaptation of artificial endosymbiosis in media could look like and what opponents could argue.

Part I: Application Scenario

1. Population and agricultural outlook

In the following section, we try to outline how world population is likely to develop by the mid and the end of this century. As population is one of the key drivers of food demand, we will also outline the trends in food demand... Additionally, we present the agricultural supply trends and prices of the world food markets. Key issues in human nutrition will be presented in the section below.

1.1. Population estimates for the 21st century

The world population is expected to grow significantly in the coming decades as Figure 1 shows. Depending on the assumed fertility rate in the future, different scenarios are given for the future world population growth (United Nations, Department of Economic and Social Affairs, Population Division, 2015b). The development of growth rates is influenced by many factors. It is a wide spread notion that economic development is a core factor influencing the total fertility rate. As incomes rise, families switch from having relatively many children with little investment in human capital in them to having fewer children and investing more in human capital (Becker, 1993).

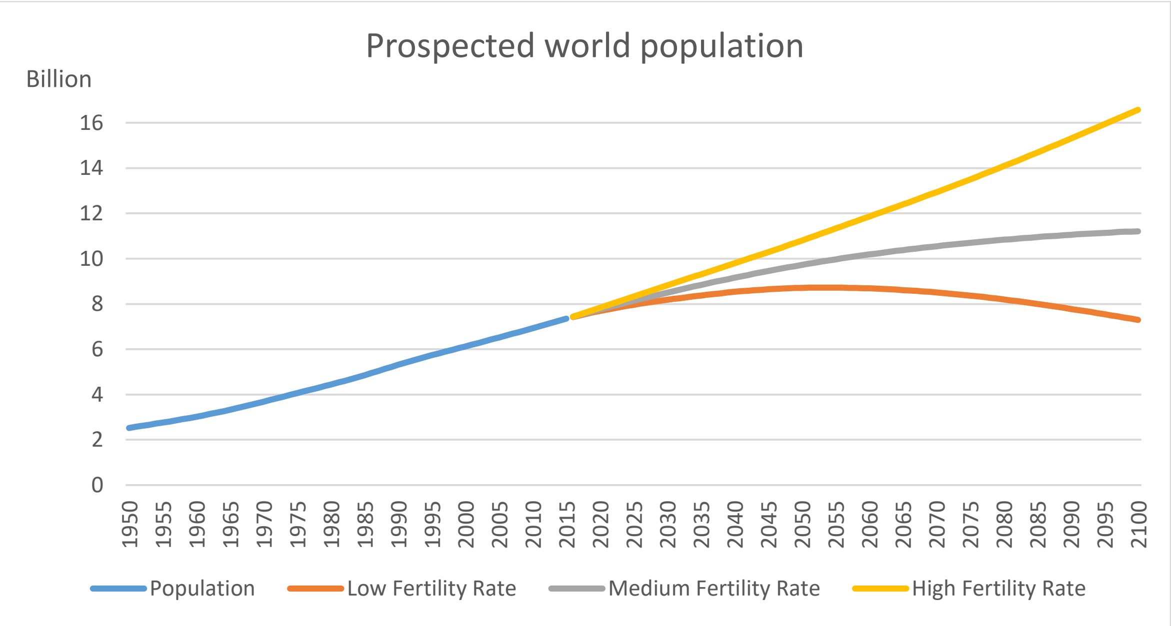


Figure 1: Observed and prospected world population until 2100.

Source: United Nations, Department of Economic and Social Affairs, Population Division (2015).

There are reports that the world is approaching the end of absolute poverty with great success in poverty reduction reported in Asia. Hauling the remaining above the poverty line of 1.25$ per day will be more difficult, but further reduction can be achieved through economic growth (The Economist, 2013).

During the last years decreasing fertility rates could be observed along with rising incomes in many developing countries. As the world is approaching "the end of poverty", population growth rates are expected to decline from 2.5 children per mother in 2015 to 2.4 in 2030 and 2.2 in 2050 (United Nations, Department of Economic and Social Affairs, Population Division, 2015a). On a global scale, the fertility rate will reach a level close to the necessary replacement rate, i.e. the rate to sustain the population. This reduces the speed of the global population growth, but due to a lag effect the rate will increase until the end of the century. Thus, the medium fertility scenario shown in Figure 1 seems to be a feasible one. This means, that we can expect world population to increase to about or slightly above 11 billion by 2100.

1.2. Agricultural outlook

In their "Millennium Development Goals" the United Nations agreed on establishing the development goal of ending extreme poverty and hunger by 2015. The target of halving the proportion of people suffering from hunger in the period from 1990 to 2015 was subsequently formulated and by 2015, the target was almost reached. The global prevalence of hunger fell from 23.3% in 1990 to a projected level of 12.9% in 2015 (United Nations, 2015). For the period after 2015, the United Nations have set the even more ambitious goal to completely end hunger in the world by 2030. The Food and Agriculture Organization of the United Nations (FAO) states that "there is more than enough food produced today to feed everyone." It is perceived as a key task to ensure sufficient and secure food supply for the growing population, which is expected to reach around 10 billion by 2050 (Figure 1) (FAO, 2016). Yet, a key issue remains in providing food for the remaining undernourished. If and how this could be achieved is described in the section below.

1.2.1. Demand patterns and outlook

Since population growth is considered to continue for the next decades, the question whether the world is running into a "Malthusian trap"[1], which is that the growth in population

[1]In his "Essay on the Principle of Population" (1798) Thomas Robert Malthus (1766-1834) postulated that the human population would grow geometrically (rising as 1,2,4,8,…) while food production would only grow

outpaces the growth in agricultural production, has often been raised in the past years. In the following paragraph we try to outline key prospects for the development in the supply and demand of food as well as key tasks to ensure a sufficient food supply in the future.

The world demand for food is expected to grow sharply over the next decades. This increase is mostly caused by the growth in population as shown in section 2.1. Especially the developing countries will face a rapid growth of their population towards the mid of the century. Another factor which will drive food demand in the future is the growth of incomes in the developing countries. As people become more affluent they tend to shift their consumption from relatively inferior goods such as staple foods (rice, wheat and maize products) towards a higher intake of meat and dairy products along with more oil and fats, fruits, vegetables and sugar which are of higher value and thus relatively superior to staple foods. This phenomenon widely observed is called “nutrition transition”. Additionally to that, a higher share of additional income is spent on food in developing countries compared with industrialised countries such as the United States. Developed countries tend to have more stable nutrition patterns. In developing countries as well as in developed countries cereals account for the largest share in daily calorie intake. (OECD/FAO, 2016). It is found that food demand is expected to grow by 74 percent until 2050 as an average of the different models examined (Valin et al., 2014). This rate is even higher than the one other scholars found. For instance, Alexandratos and Bruinsma, (2012) find an expected annual growth rate of 1.1 percent on a global scale for the period from 2005/2007 through 2050. This roughly equals a demand growth of 54 percent until the end of their projection period.

1.2.2. Recent developments in supply and future prospects

Although the overall nutritional situation has significantly improved since the latter half of the last century, despite demand growth, there are some more challenges the world is facing in the foreseeable future: Over the past decades the world has experienced a sharp decline in the arable land per capita as Figure 2 shows. Some high income countries tend to be rather abundant in land endowment suitable for crop farming (United States, Australia). Yet, important European countries such as Germany have a comparably low per capita endowment of arable land. Many nations from Middle-East rank even lower, as does China. Equalling 0.57 ha, estimates for the area (hectares per person) under cropping activities in

arithmetically (rising as 1,2,3,…). This would eventually lead to starvation and a shortage in food supply without effective birth control in place in order to limit population growth.

Sub-Saharan Africa on the other hand are relatively high in a worldwide comparison. In total, in the beginning of the nineteen-sixties, there were 0.37 ha available per person whereas today per capita land endowment on a global scale is only 0.20 ha (The World Bank, 2016).

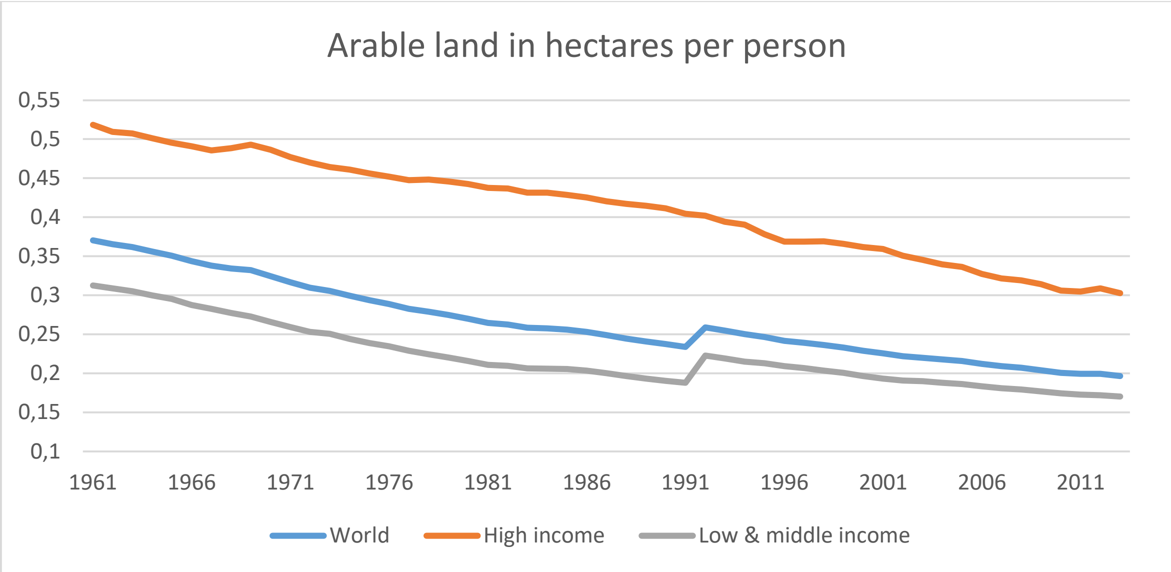


Figure 2: Arable land in hectares per person from 1961 to 2013 for high income, low & medium income countries and the world.

Source: The World Bank (2016)

Global patterns in food supply are reflected through international food prices. Figure 3 shows a time series of commodity prices for the three main staple crops in human nutrition. Prices are given in U.S. Dollars per metric ton and correspond to the prices of wheat (No. 1 Hard Red Winter) observed in Kansas City, the price of maize (U.S. No. 2 Yellow) at the Gulf of Mexico and the nominal price quote of milled white rice in Thailand. All prices have been retrieved from International Monetary Fund (2016). These locations represent major exporting countries for the three commodities. Thus, they can be seen as an indicator for the world market prices of these goods[2]. Generally, one can find that prices tended to slowly decline until the middle of the last decade. In 2008 and 2011, two price spikes can be observed. A period of more volatile prices can be found from 2008 onwards with a period of falling prices following since the late 2012.

[2] Due to transportation costs, administrative costs and other factors, domestic prices differ from the given commodity prices. Therefore, there is no single world market price observed by all countries, but different import or export prices which are strongly correlated with the given series.

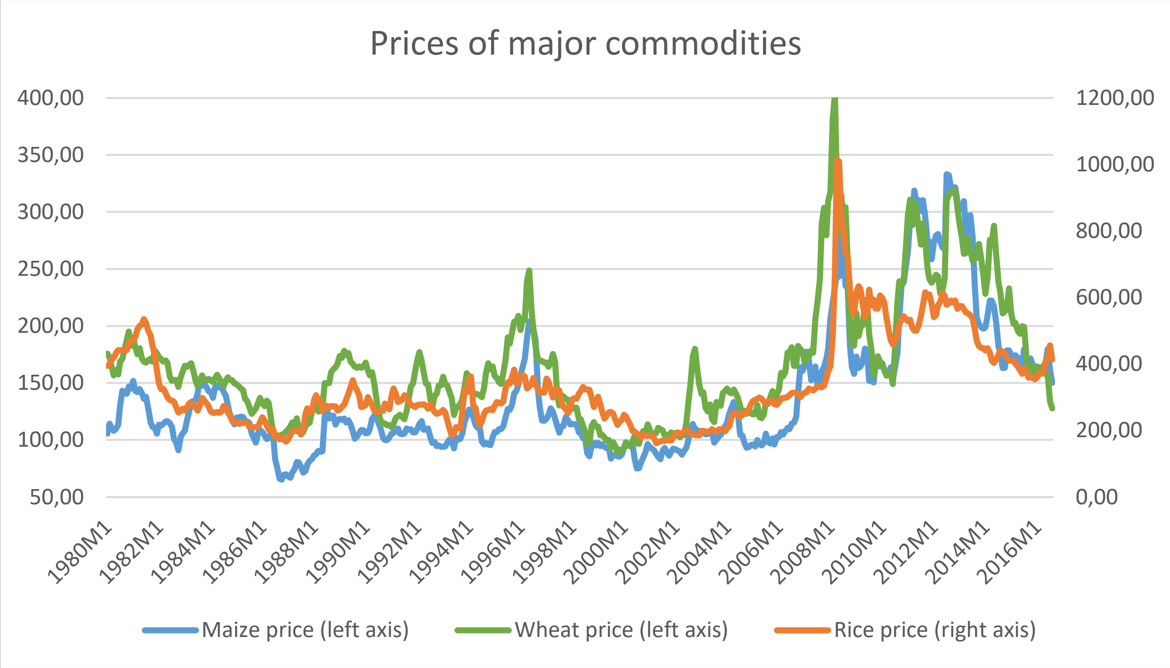


Figure 3: Time series of prices for major food commodities in U.S. Dollar per metric ton observed in leading export regions.

Source: International Monetary Fund (2016)

The causes of these price spikes have been widely discussed in literature. A set of feasible causes was lined out by different authors. Policy interventions and the depreciation of the U.S. Dollar were found to be likely causes along with rising oil prices. The increased production of biofuels is regarded as a major driver in commodity prices, since it increases demand for maize in the United States and oilseeds in the European Union. Favourable demand conditions for these goods lead to reallocation of land towards the production of biofuels away from other crops. Thus, first generation biofuel production tightens supply of major staple crops and thereby leads to increasing food prices. Following the time around 2005, when biofuels were heavily promoted in the United States and the European Union, an sharp increase in corresponding commodity prices can be observed ((Headey and Fan, 2008), (Mitchel, 2008) and (Trostle, 2008)).

Along with the abovementioned factors, food supply will be influenced by production trends. The daily amount of calories that is on average available to human consumption is likely to even increase until 2050. Sources for this future production growth are seen mainly in yield increases and to some extend in higher cropping intensities. Moreover, some suitable land, mainly located in Sub-Saharan Africa and Latin America could be brought into cultivation. Nonetheless, this land suffers from constraints, such as lacking infrastructure or increasingly high ecological cost of land use change (Alexandratos and Bruinsma, 2012). There are

several issues stated in literature which are to be overcome in order to sustainably increase food supply. Main objectives are first to close the "yield gap", which is the difference between the best potential yield using available gene material and production techniques and the actual obtained yield. Second, to increase production limits also utilising genetically modified organisms. Third, to reduce food loses due to waste and a change in diets towards a more plant based calorie intake instead of animal based products (Godfray et al., 2010).

2. Land Grabbing

There are several figures about the extent of land grabbing found in the literature. These figures vary widely due to different periods covered and ways the data is obtained. One frequently used source is the "Land Matrix Initiative". They present an overview of finalized, intended and failed land deals of more than 200 ha. As of October 2016, there was an area of 47,648,465 ha involved in finalized deals (Land Matrix, 2016b). This equals to about one percent of global agricultural land. In the section below we try to outline the basic concept of land grabbing and its reasons, targets and linkages to the aforementioned development. We will furthermore outline the mechanisms our lab projects try to tackle and overcome.

2.1. Definition of land grabbing

The term "land grab" and the process of "land grabbing" have gained public interest after the food price spike described in section 1.2.2. Land grabbing refers to the surge in international commercial land transactions aiming for the large scale production and exports of food and biofuels in the last years. It builds on the concept of (Northern) corporations and governments investing in third countries and thereby enclosing commons and the expropriation of peasants and indigenous people (in the South[3]) (Borras Jr and Franco, 2012). The authors state that the expression suffers from some weaknesses, since it has been coined by activists to highlight the need to counteract the process of land acquisition. A de-politicized term for "land grabbing" can be seen in the term "large-scale land investments" and other alike expressions (Borras Jr and Franco, 2012). Large-scale acquisitions are purchases, leases and other forms of land use rights transfer regarding areas of more than 1000 ha (Cotula et al., 2009) or an even bigger area such as 2000 ha as a minimum size

[3] Here the concept of the Global North, which are developed industrialised, predominantly located in the northern hemisphere and the Global South, developing countries, which are predominantly located in the southern hemisphere, is meant.

(Schoneveld, 2014)[4]. The two terms land grabbing and large-scale land acquisitions are used synonymously throughout this report.

2.2. Reasons for land grabbing and widely observed patterns

A wide discussion on the main driving forces of land grabbing has taken place in the public, political and scientific world following the 2008 food price spikes. In the following section we will present reasons for land acquisitions, the role of biofuels in it and outline main target countries of investments.

2.2.1. Food security as one driving force of land grabs

As Figure 3 shows, the world has experienced severe price spikes of major food commodities in the year 2008 and a period of high and volatile prices from 2011 until about 2014. The 2008 surge in food prices has raised concerns about food security in investor countries (Cotula et al., 2009). Their argument of food security issues is followed by many authors. Braun and Meinzen-Dick (2009) find that export restrictions in producing countries during periods of high prices have raised food security concerns in importing countries. A distrust in international markets is seen as one reason for countries to search for other means of food supply by land grabbing. Countries that are acquiring land internationally are found in the Gulf region. Main driver in this case is the scarcity of natural resources in terms of arable land and more importantly water resources for irrigation.

Moreover, countries with large populations and relatively low amounts of arable land such as China, India and South Korea contribute to land acquisitions as investors. Deininger and Byerlee (2011) share their view of land and water scarcity as one driver of land grabs. Anseeuw et al. (2012) and Cotula et al., (2009) find the expectation of rising food prices, growing world demand and increasing food demand make agriculture a more interesting investment. Therefore, the factors presented in section 1 of this report can be seen as leading driving forces behind the emergence of land grabs in the last years since 2008.

2.2.2. The role of biofuels in large-scale land acquisitions

Although biofuels are not the only factor for driving land grabs, yet they are considered to be one important factor in land acquisitions. In 2014, there was an area of 3.8 million ha for

[4] Land Matrix assesses land acquisitions above 200 ha. Note, that there is no single convenient definition of a size at which a transaction is considered to be large. This is one reason why the figures on acreages involved in land grabbing activities widely differ among different sources.

pure biofuel use and additional 4.4 million ha in “mixed” deals (crops that can potentially be used for biofuels and other uses, e.g. soybeans) under contract in large scale land acquisitions. This equals to about 23 percent of all large-scale land deals (Nolte et al., 2014). Biofuels are promoted through mandatory blending quotas in the United States (bioethanol) and the European Union (biodiesel). Thus, they do not only have effects in the regions they are promoted. By rising prices through increased demand they also have effects on land use change in other countries. Along with slower growth rates in production, greater resource constraints and the dietary changes and population growth described in the previous chapter, land will remain a target for future investments (Deininger and Byerlee, 2011).

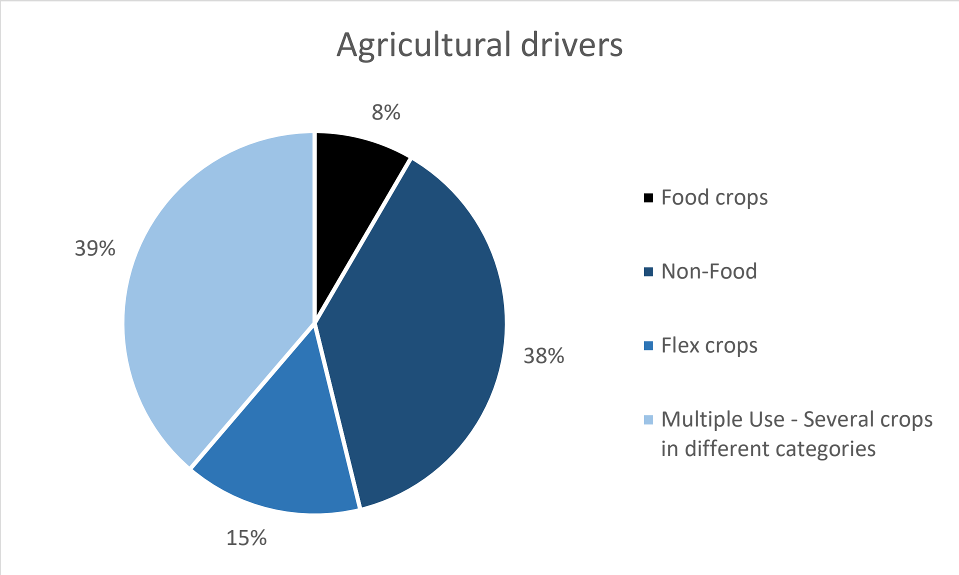


Figure 4: Shares of the main agricultural drivers in land grabs as of October 2016.

Source: Land Matrix (2016a)

Figure 4 shows the share of the main agricultural drivers of land grabbing as they are stated by Land Matrix. The platform lists shares and acreages for the according category of product as a sum of different projects for which data on the purpose is available. Pure food crop projects have a minor share in overall projects, while non-food crops and flex crops, that both can be partly or totally utilised for industrial purposes as in biofuel production have significantly higher shares in large scale land acquisitions (Land Matrix, 2016a). Other scholars support the view that biofuels are a key driving factor in international land grabs. Most of the land acquisitions did not primarily target food production, but rather have biofuels and industrial products as main outputs (Borras Jr and Franco, 2012), (Deininger and Byerlee, 2011), (Cotula et al., 2009) and (Nolte et al., 2014). Investors that seek biofuel production are found in the group of developed countries. The Netherlands, Great Britain,

Canada, France, Italy and Spain are the main origins of investments in biofuel production through land acquisitions. The rush for land for pure biofuel products is reported to be over. Investors switch to projects focusing on more flexible outputs which can be used in biofuel production along with other uses such as animal feed or in human nutrition (Nolte et al., 2014). This is a trend that is also reflected in Figure 4. About 60 percent of all investments focus on oilseeds. In Africa, Jatropha, an inedible yet to be domesticated oilseed plant that can be grown on marginal lands using minimal inputs, accounted for about 30 percent of all investments. Its only use is the production of biofuels. Unlike oil palm and sugarcane projects with multiple uses for their outputs, Jatropha projects failed in most cases (Schoneveld, 2014). Nonetheless, multi-purpose output projects are favoured instead and thus biofuels still are a matter of consideration for investors.

This highlights that land grabbing is a multi-facetted phenomenon with many factors being interdependent. Biofuel production can lead to rising food prices, which in turn raise concerns about food security. Along with governmental incentives for biofuels, securing food supply makes investments in land in third countries attractive.

2.2.3. Target countries for land grabbing

There are some characteristics target countries for land grabbing commonly fulfil. When looking at the conditions of agricultural production, one can find two distinct patterns. First, that there is a large gap between actual obtained yields and the potential yield, which is called the “yield gap”, as already described in the previous sections. Second, that there is the potential for land expansion. Target countries have suitable land available that can be brought into cultivation in the future ((Deininger, 2011), (Deininger and Byerlee, 2011), (Anseeuw et al., 2012)). The latter authors also find that investors tend to invest in areas with good accessibility. This is due to the fact that inputs such as fertilisers, seeds, pesticides and machinery need to be available for intensive production. Moreover, good accessibility ensures market access for the produce. Producers can rely on existing road infrastructure for their production.

The above mentioned patterns can be widely observed in Sub-Saharan Africa. Yield gaps found in the region are the biggest on a global scale. Thus, there is scope for improvement in production through foreign investors. In some relatively land abundant countries in Sub-Saharan Africa, there are land resources that can be brought into cultivation. Therefore, the international focus of land grabs is on Sub-Saharan Africa ((Deininger, 2011), (Deininger

and Byerlee, 2011)). This reflects findings in section 1.2.2, which find most potential for production increases in the said region both in terms of closing the yield gap and through area expansion.

In Sub-Saharan Africa only six countries account for more than half of area involved in land grabbing. These six target countries are: Ethiopia, Ghana, Madagascar, Mozambique, South Sudan, and Zambia. The area involved on land deals in these countries amounts to 1.5 million ha. The countries cover only 17.0 percent of Sub-Saharan Africa's land area (Schoneveld, 2014). Aside from general underlying patterns, the author cannot find a clear explanation, why the deals are strongly concentrated in a few countries. This shows, that the occurrence of land grabs has many specific reasons and is not easily explained by only a few factors.

2.3. Concerns and possible problems arising from land grabbing

Large scale land acquisitions can be a chance for investment in agriculture and thereby promote rural development. Possible positive effects can be the creation of on-farm and off-farm jobs and the provision of rural infrastructure, schools and health care services (Braun and Meinzen-Dick, 2009).

Yet, land transfers can be linked to effects that rise concerns about their legitimacy. It was found out that investors often acquire land in countries and regions with weak land tenure rights (Deininger and Byerlee, 2011), (Deininger, 2011). Weaker land governance regimes are significantly more likely to attract land investments (Arezki et al., 2015). This is especially the case for Sub-Saharan Africa where most of the land is formally state owned. Governments cannot provide secure land-related property rights due to dual rights systems. There is the aforementioned formal state ownership of land rights in Sub-Saharan Africa as great areas are used as commons and a simultaneously existing customary land rights system in the regarding countries. The lack of formal recognition of the customary land rights may deprive local populations from access to the land they used under the customary regime. Moreover, in some cases, local leaders who play a key role in the reallocation of land rights fail to act in the interest of the community they lead (Anseeuw et al., 2012). Even those Sub-Saharan African countries with comparably far reaching recognition of customary land rights, e.g. Tanzania and Uganda, make it hard for ordinary landholders to secure and defend their interests in the land they live on. Governments are reluctant to give up their position as majority land owners. There are interwoven elite interests and the governments lack will to deprive themselves from the ability to reallocate land resources. The land laws are not found

to be the driver of dispossessions, but to facilitate them. Thus, rural poor can be excluded from an important resource for their income which is the common land of a community that is regarded as not privately owned state land under the legal framework. Since the Sub-Saharan countries are not yet industrialised to an extend that is able to absorb the rural labour force that is driven from their previously customary owned land there is potential for arising conflicts (Alden Wily, 2011).

The above mentioned threads to the livelihoods of rural communities is of concern for many Non-Governmental Organisations (NGOs). Since the sharp increase in large scale land acquisitions following the 2008 food price spikes, there has been a significant number of campaigns focusing on the complex of land grabbing. The issue of land rights and the thread of expropriation and eviction of indigenous people from their commonly owned land has raised concerns of major international NGOs. In one of their latest releases on the topic, Oxfam finds drastic words:

> *"Oxfam's latest land rights campaign focuses on cases typical of the escalation we can expect. Women left behind. Rights ignored. Entire communities evicted from their homes. We are in the midst of the single biggest attack in the world today on people's identity, rights, livelihoods and security, as well as our environment. They cannot afford to lose this fight, nor can we."* (Oxfam, 2016)

Another notable NGO which is dealing with the topic of land grabbing is GRAIN. In 2008, this NGO was one of the first that reported about the then new wave of large scale land acquisitions. Since then GRAIN has held a strong position against land grabs all over the world. Until mid-2016, the organisations counts 491 land deals covering an area of about 30 million ha in 78 countries (GRAIN, 2016). GRAIN opposes the expansion of agribusiness companies into areas that are known to be the target of land grabs. It is one objective of the organisation to promote rural smallholder farming in developing countries, which they see to be endangered by land grabbing.

One should be aware that NGOs like GRAIN and Oxfam use drastic expressions and a strongly negative picture of large scale land deals in order to raise funds for their operations. Nonetheless, many of their findings are backed by the study results obtained by independent researchers as shown above. Especially the danger of enclosure of commons facilitated by weak land rights regimes is highlightened by many scholars.

3. Synthetic endosymbiosis as a tool to overcome land grabbing

In the following section we try to outline the benefits of synthetic biology for the production of organic outputs suitable for biofuel production. The basic concept of synthetic endosymbiosis is presented. Furthermore, an overview of the obtained achievements of the corresponding lab project are shown in the section below. We show a roadmap of the steps that are yet to be fulfilled in order to achieve fully functional synthetic endosymbiosis generating outputs suitable for biofuel production.

3.1. General problems in establishing synthetic endosymbiosis

Probably the most generic problem in overcoming large scale land acquisitions due to biofuel production is the efficiency of secondary plant substrate production by microorganisms. Even though it is possible for most products of interest, it generally requires a lot of genetic modification to the organisms. This includes the overexpression of endogenous as well as exogenous proteins suitable for the desired process and the utilized organism involved in the process. However, it can take several years of research and a lot of money to successfully express a production pathway in a microorganism. Additionally, through the expression of these genes it is likely to create so called ‘bottlenecks,’ which lower the production efficiency by an accumulation of intermediates through low enzyme activity. All in all, genetic engineering always rises the so called ‘metabolic burden’ of a cell, meaning that energy requirements for the essential processes for growth and metabolism cannot be met.

3.2. How to circumvent bottleneck situations

Our aim was to bypass such bottlenecks in the production of biofuels or pharmaceuticals derived from terpenes by distributing synthesis steps and thereby the metabolic burden to several organisms. By distributing synthesis steps according to the strengths of the employed symbionts we are able to circumvent occurring bottlenecks in the whole pathway. As soon as there is a bottleneck occurring within one organism, another one which is better in processing the substrates simply takes over. We accomplish this through a fusion of two model organisms into each other – a principal called ‘Artificial Endosymbiosis’ – which requires following steps, illustrated in Figure 5:

1. The establishment of a dependency between the organisms
2. Splitting and implementation of the desired production pathway into the organisms according to their strengths

3. Fusion of the cells

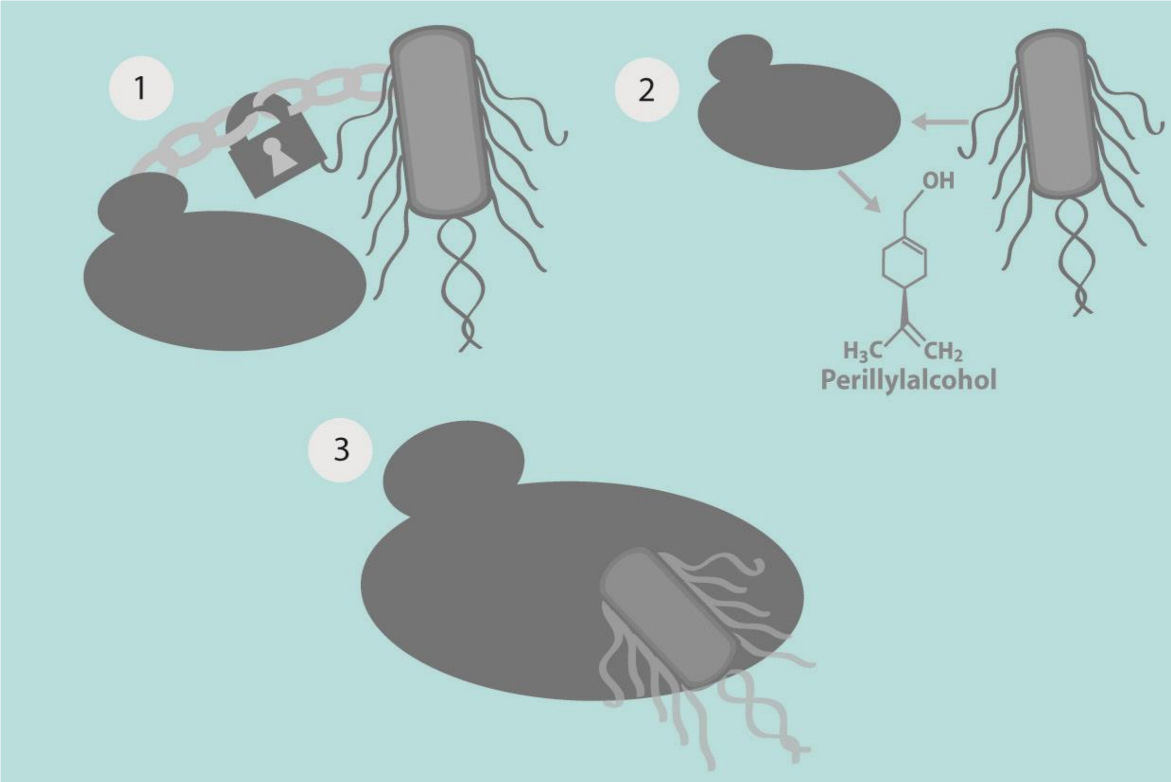


Figure 5: Schematic overview of the three crucial steps for establishing artificial endosymbiosis shown for S. cerevisiae and E. coli. (1) The introduction of a stable dependency to ensure mutual growth. (2) Implementation of the desired production pathway into both organisms, here with the product perillyl alcohol. (3) The actual fusion of the cells, mediated through polyethylene glycol (PEG).

Source: Own work

In the beginning of this process, one has to decide for pertinent organisms which are most likely to perform the desired production task. In our case (and to proof our concept), we chose two of the most well-known model organisms in microbiology: *Saccharomyces cerevisiae* and *Escherichia coli*. Because these cells are perfectly adapted unicellular microorganisms, they are unlikely to form a symbiosis between each other. Due to this, a dependency between the organisms has to be established. We have decided to solve this through a malonate exchanged based dependency in which *S. cerevisiae* cells are deficient for the production of malonate. Malonate, or respectively its thioester Malonyl-CoA, acts as a key player in the synthesis of fatty acids. This pathway is essential for the cell and is needed for instance for the synthesis of cell membranes.

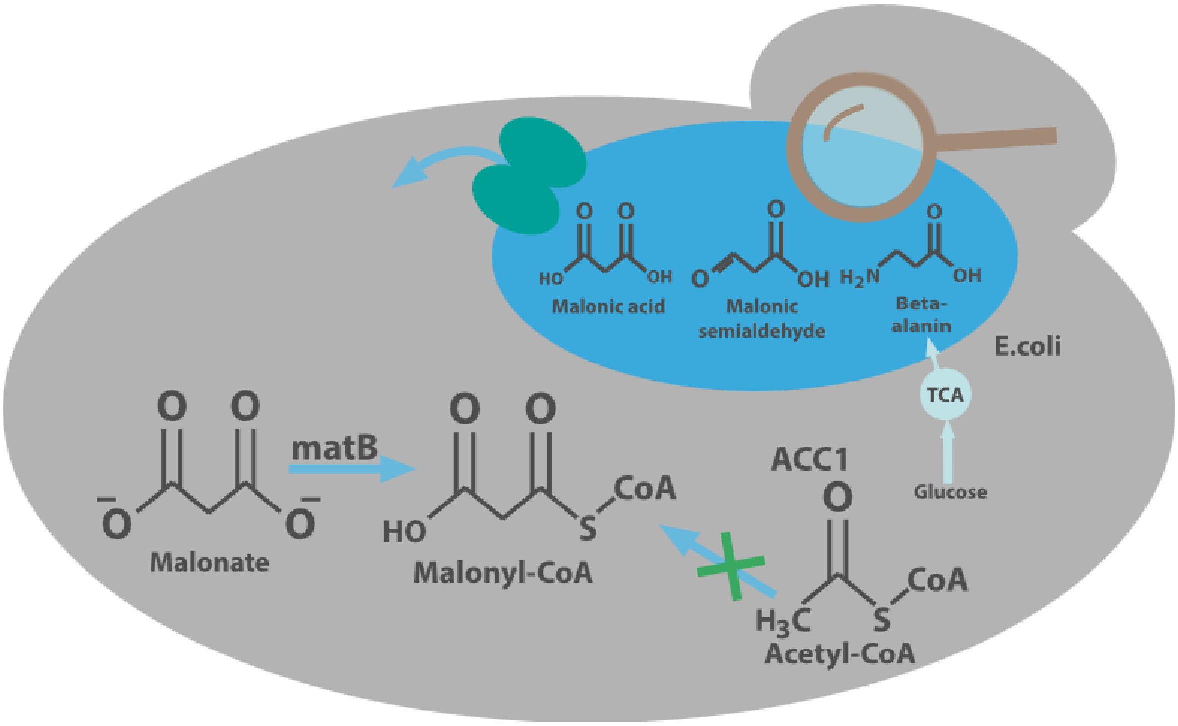


Figure 6: Building up dependency between organisms using malonate

Source: Own work

Since our yeast cells are unable to synthesize malonate themselves, it is being produced and secreted through *E. coli* as shown in Figure 6. By this, we set up a selection pressure in which only those yeast cells that have taken up *E. coli* are able to grow. To ensure the survival only of those *E. coli* which actively participate in our system and that are located inside the yeast we adjusted the pH of the medium to approximately 4. *E. coli* is not able to live under these conditions in contrast to yeast, which can tolerate a wider range of pH values and continues to grow. Thereby only *E. coli* cells inside yeast are able to survive.

The second crucial step in setting up this production system is the implementation of the pathway itself. Because not every enzyme has the same activity in every organism (Na et al., 2010), the search for the most suitable enzymes is mostly expensive and time consuming. Since our system is using different organisms, this problematic search is reduced to a minimum by simply using the organism's strengths and adapting the engineering of the production pathway according to this. For example, if an intermediate within the pathway is toxic to yeast, we set this as the point where *E. coli* takes over the synthesis by expressing the following parts of the pathway in *E. coli*. This needs to be ensured through the active transport of the intermediates between the organisms.

To proof this, we implemented the production of the terpenoid limonene, a highly valuable monoterpene for the production of chemical and medical compounds, into *E. coli*. This mechanism is well known (Alonso-Gutierrez et al., 2013), so we added some following steps: at first, the export of limonene out of *E. coli* into yeast. Next, the ability of yeast to utilize the limonene and convert it into perillyl alcohol and then secrete this into the medium. Figure 7 illustrates this process. Although both the production of limonene as well as its conversion to perillyl alcohol have been described before in one organism (Alonso-Gutierrez et al., 2013), we aimed for increased productivity using our novel method with a division of labour between two different organisms.

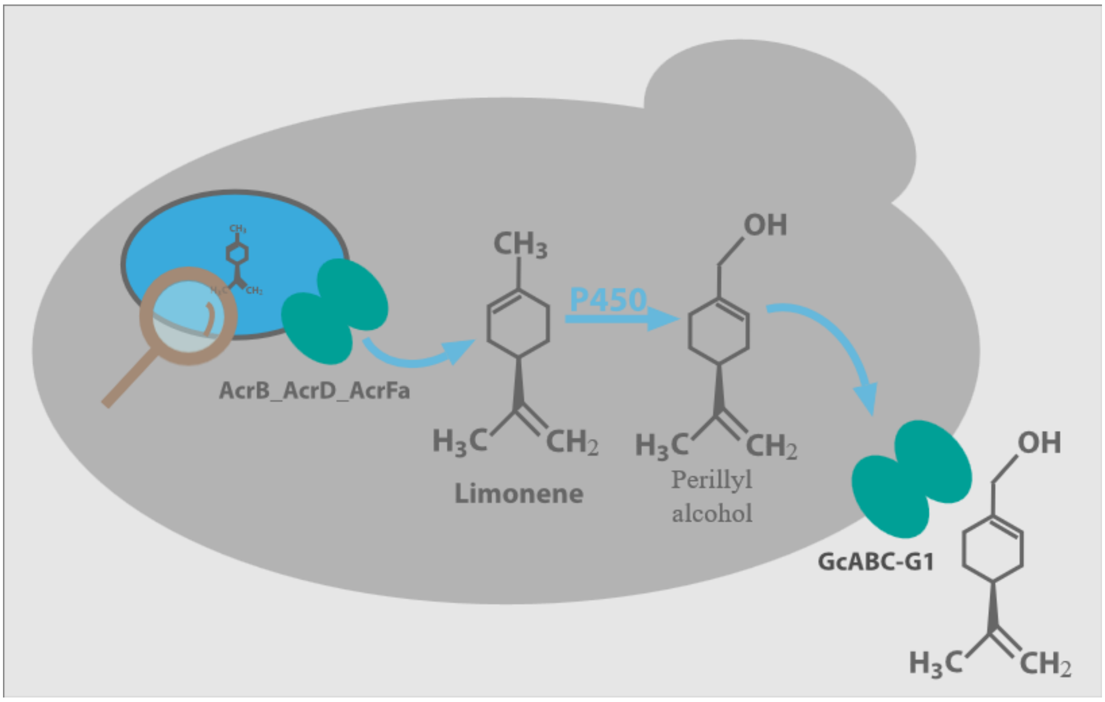


Figure 7: Synthesis and secretion of limonene and perillyl alcohol

Source: Own work

The last challenge of our project is the actual fusion of the organisms themselves. Different methods to accomplish this have been described within the past decades and can be divided into two groups: the active mechanisms where the symbiont actively either gets taken up or introduces itself into the host (Agapakis et al., 2011) on the one hand or the passive mechanisms, in which the symbiont gets injected or is fused to the host on the other hand (Yamada and Sakaguchi, 1981). Since the latter do not require any genetic modification regarding the fusion, we decided to use a passive fusion mechanism which is applicable to a variety of organisms. This method consists mainly out of three steps. At first, the yeasts cell wall gets digested using an enzyme called Zymolyase, which cleaves the β-1.3-glucane

bonds and leaves the yeast cell only enclosed by its lipid membrane. Because lipid membranes can be fused, the endosymbiont has to be encapsulated by a lipid membrane, too. For this, we use polyethylenglycol (PEG) of different molecular weights. PEG is an oligomer of polyether and able to form a so called 'liposome', a membrane-like vesicle around the organisms. Even though the actual mechanism is still unclear (Guerra-Tschuschke et al., 1991), bringing these two lipids into spatial proximity most likely leads to a fusion of the membranes, where the original yeast cell still is the main compound. Due to this, yeast is able to regenerate its cell wall, after which the whole procedure is finished.

3.3. Remaining challenges in establishing artificial endosymbiosis

Even though the system described above provides a great opportunity to replace the production of valuable secondary plant substrates through land grabbing by using microorganisms, there is still a big issue to solve. One of the key compounds for micro-organisms for growth and metabolisms is a source of carbon, mainly sugars such as glucose or sucrose. Since these are usually obtained from plants as well, the issue of land grabbing could not be targeted using our system in the current stage. To solve this, we are planning to implement another organism into our system, yet in a different way. The used organism is a cyanobacterium that is photosynthetically active. This means, it is able to produce sugar out of CO_2, water and sunlight.

Since certain cyanobacteria are known to accumulate sugars as a protectant to osmotic stress, they can be modified to secrete these sugars into the medium, which then can get taken up by *S. cerevisiae* and *E. coli*. This is achieved through overexpression as well as deletion of several genes involved in the accumulation of osmoprotectants. Most commonly used cyanobacteria share the same set of homologous genes suitable for the production of sucrose, namely *sps*, *spp* and *ugp*. In addition to the deletion of a gene called *ggpS*, which is a key player for the production of an osmoprotectant that cannot be utilized sufficiently by yeast or *E. coli*. This leads to an 4-fold increase of intracellular sucrose accumulation and has been shown to work with several cyanobacterial strains (Du et al., 2013), (Ducat et al., 2012). The secretion of the accumulated sucrose into the medium is enabled through the expression the sucrose permease dependent exporter CscB.

To provide this sugar as a carbon source directly to the fused *S. cerevisiae* – *E. coli* symbionts, the cyanobacteria can be linked to the surface of the host. This is enabled through the expression of so called 'leucine-zippers' on the surface of yeast as well as cyanobacteria.

If these zippers are brought into proximity to each other, they form a stable bond and the yeast and *E. coli* are being provided with sugar for their metabolism.

4. Conclusion

The artificial endosymbiosis, as described above, is not likely to be able to offset land grabbing as a whole. We can tackle land grabbing that occurs due to biofuel production. The report shows that the majority of land that has been sold or leased to foreign investors in the recent years is either used directly for biofuel production or for flex-crops like oil palms. These crops allow the production of biodiesel as well as vegetable oil or other products for human consumption. Flex crops and direct biofuel production are the two groups of projects artificial endosymbiosis should focus on. During the next several decades the world population will keep increasing and through theincome growth in developing countries the nutrition transition will also persist. In other words, the pressure posed on arable land by this will remain high in the long run. In Sub-Saharan Africa and in South America, there is still the possibility for area expansion since uncultivated land can be found in these regions. Nonetheless, environmental costs of bringing new land into cultivation is increasing because there is a conflict between human nutrition and environmental services provided by the uncultivated land. Production in bioreactors could also partly avoid these environmental costs from occurring because less additional land needs to be brought into cultivation.

Since the system of two fused organisms and a “zipped” cyanobacterium   has yet to be established, forecasts on the production efficiency in terms of tons of output per unit of land or in kilojoule of usable energy per unit of land cannot be made yetThus, comparability with recent agricultural practices are limited. Still, we try to outline possible applications once the process is introduced into markets.

4.1. Economic and regional patterns determining application

One can say that the production of biofuels through microorganisms would bind high amounts of capital since production facilities such as secure bioreactors and fermenters are required. Our production in bioreactors method could rely on already existing parts such as bioreactors, glass pipes and separators. Another asset of the new method would be that it is not bound to a certain type of land. That is, it can be built on land that has no other uses such as ruderal spaces, very marginal land not suitable for agriculture or even off-shore. A system that provides carbon through photosynthesis by attached cyanobacteria mainly needs

photoactive radiation as a source of energy. To ensure environmental sustainability in this case solar radiation should be preferred. Artificial sources of light need electricity, which is not necessarily generated from renewable sources. Moreover, conversion losses can be avoided using direct sunlight. Given that infrastructure for the transport of the product is provided, the system is likely to work best in global areas with high solar radiation. Therefore, regions located further towards the tropics could be suitable for biofuel production through artificial endosymbiosis. These regions, such as Sub-Saharan Africa, unfortunately often lack infrastructure, but they are the regions where land grabbing is frequently observed nowadays. Since there are no requirements on land quality, production facilities could be built in urban or peri-urban areas which lifts the infrastructure constraints to some extent. Investors could possibly draw on existing networks for the logistics and marketing regarding biofuels. This could facilitate market entry and linkage to main consuming regions for biofuels such as the United States and Europe. Possible positive side effects could be the promotion of industrialisation of developing countries and increased investments in low income countries which create employment opportunities. Moreover, land acquisitions are relatively expansive, although land prices in Sub-Saharan Africa are among the lowest on a global scale. High-yielding agriculture strongly draws on the use of machinery and technical equipment. Furthermore, inputs like fertilisers and pesticides need to be bought in. All of this makes mechanised modern agriculture a capital intensive sector. Production in bioreactors could become favourable once the return on the capital employed at a certain risk level is at least the same as for an alternative investment in agriculture for biofuel production.

4.2. Political factors influencing the application of production in bioreactors

We find that many European countries are not likely to be a host country for investments involving artificial endosymbiosis for three reasons: First, Northern European countries lack high solar radiation which is crucial for efficient high yielding production. Second, regulatory burdens are very high. On the one hand, this would ensure secure production. But on the other hand this implicates high regulatory costs for possible investors which can make an investment unattractive. Third, in many industrialised western countries, there is a steadily high or even rising scepticism about genetically modified organisms (GMOs). The adoption of GMOs has failed in Europe so far due to public protest and there is a wide coalition of NGOs and political parties opposing GMOs. The protests accompanying the market introduction of GMO crops in agriculture could repeat as companies try to introduce

production in bioreactors which is making use of artificial endosymbiosis. Thus, research may still take place in developed countries as research infrastructure is already existing and knowledge has been build up over the past decades. Production could as well be located in countries having more favourable natural, public and administrational conditions.

North America has shown a more open attitude towards the adoption of GMOs in the past. Thus, we expect application in the United States or Canada to be less problematic. Just like the European countries they are relatively abundant in capital. Therefore, investments could not only have financial backing from Northern American institutions but North America could also be host to investments in production in bioreactors. Moreover, these countries constitute a place valuable research on the topic can take place in drawing on the existing research infrastructure.

4.3. Human impact

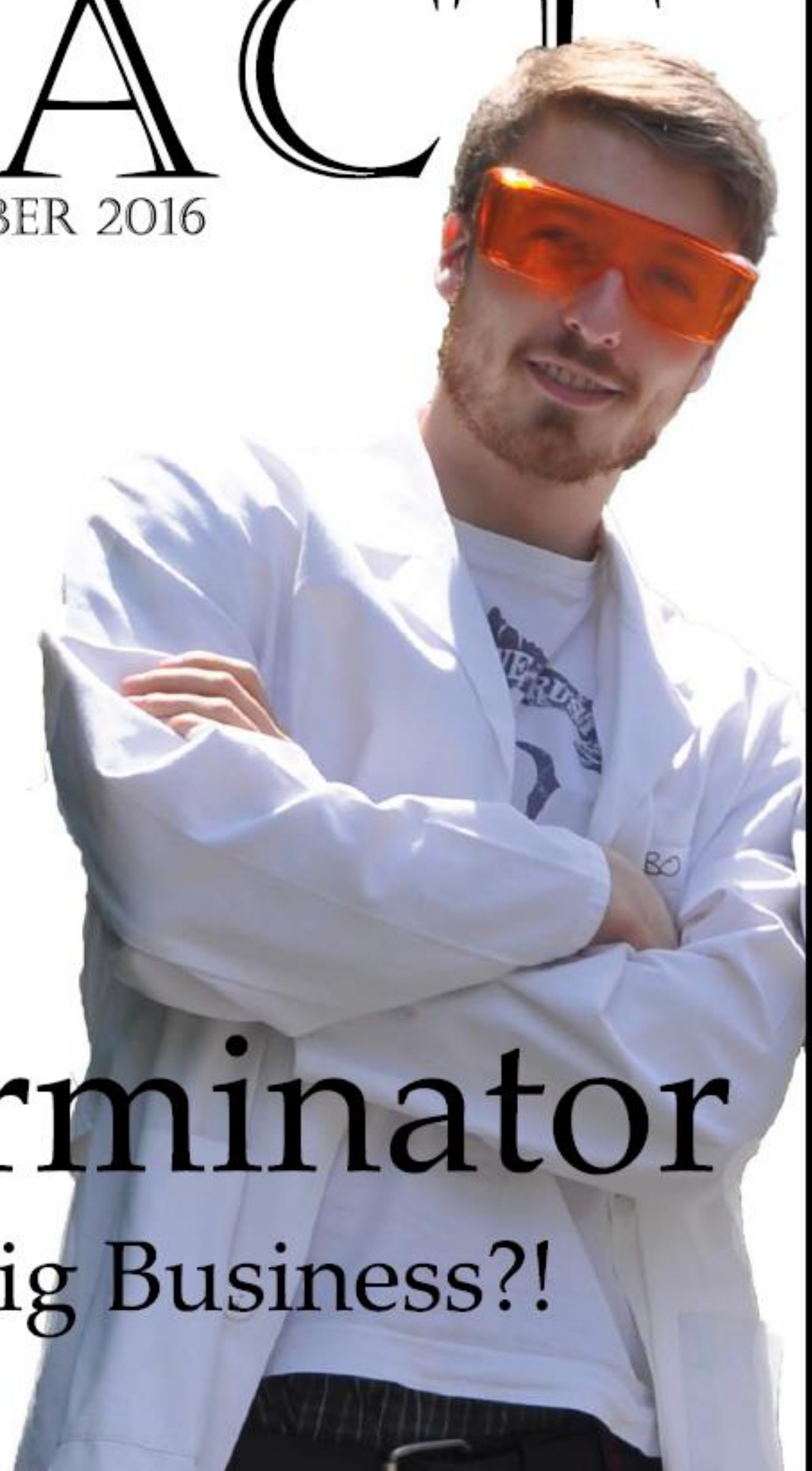
We hope that finding another source for the generation of organic matter for biofuels through artificial endosymbiosis can lift one of the most severe impact of land grabs in Sub-Saharan Africa: Dispossession of customary owned land and enclosure of commons. More efficient production methods for biofuels would reduce pressure on the corresponding commodity markets e.g. for palm oil, sugar (from sugar cane), maize and soybeans. Thus, we hope to reduce financial incentives to bring new land into cultivation for biofuels. As it becomes less attractive to create new conventional production sites, we hope that dispossession and enclosure of commons will appear less frequently in the future. This means an indirect protection of indigenous people through market mechanisms. We know that given the projected developments shown in sections 1.1 and 1.2 hold true, a total offset of new farmland creation is not feasible. Yet, we strongly believe that thinking of new solutions such as artificial endosymbiosis is crucial in limiting negative effects on local populations.

Part II: Techno-Moral Scenario

Scenario I: Ferminator: Big Business?!

FACT

OCTOBER 2016



Ferminator

Big Business?!

Ferminator Incorporated in FACT.

Imagine a company, ranked on the same level as Apple, Merril Lynch and Legal & General, a company that is part of an exclusive club of bulging wallets that control the fortunes of the world. Now think of this company as a seed planted as a small but clever idea risen as impressive as the changes that it brought to our world.

Ferminator Incorporated is a company whose name has already succeeded its original meaning. The name stands for a new product branch, invented, realized and established by the company itself. With the help of new fermentation methods, biofuels were finally able to succeed the long lasted reign of fossil fuels. A new era was born. The era of sustainability.

Ferminator is success story unlike any other. Born from a simple idea, founder and CEO of Ferminator Incorporated Steffen Lütke realized the potential of this idea. The fire that this little spark could ignite. Complex at first sight the idea was actually simple but genius. If one cannot handle the work, split the duty.


Steffen Lütke, CEO

To increase efficiency fuse them. Artificial Endosymbiosis is the secret behind Fermnator Incorporated. If you are interested in the scientific background, you are welcome read our review article about the "Ferminator principle".
Much had to happen to made Ferminator Incorporated the company it is today. Let us go back in time in 2016, specifically the small German city Marburg, where everything started.

It all started as a project of the 2016 iGEM-Team Marburg. This small seed will eventually sprout and rise to the billion-dollar company. At this time, it it is still no more than a rough blueprint of an idea.

„It started in a small town in Germany!“

But as the future shows, there is potential. That said it is no wonder that shortly after the giant jamboree in Boston that is part of the iGEM contest, the project gained attention from representatives of economy and research. About half a year later, Ferminator Incorporated appears as a registered and protected trademark. In the next 5 years several research centers in Munich, Frankfurt and Marburg open. At this time the company is counting 75 employees. Most of the project's funding comes from research funds and brave investors who not only believe in the idea but also in the team. Prototypes are developed and first successes are recorded. At this state the company is claiming its first patents and expands dramatically. In 2021 the first Bio production site is taking in operation. It is located in Brasil and is heartwarming welcomed equally by economy, politics and society. It was originally planned to be built in its hometown Marburg, but due to complex law and suboptimal sunlight conditions, it was decided to transfer the reactor to the beautiful coast of brasil. At this point it needs only 5 more years until the first commercially used reactor opens. The opening ceremony marks the start of perspective changes and the beginning of the dominance of "Biofuels".
By the end of 2030 Ferminator Incorporated is an indespensible constant in the world economy and dictates growth and changes in global trading of biofuels. In over 20 research facilities spread over three continents bioreactors are providing enough energy and biofuels to cover demands of the majority of mankind.
The patented endosymbiosis method is highly efficient in producing 'high value low amount' substances. Multiple new research sites all over the globe are established and the first prototypes are being produced.
To this day, 24 years after the launch of Ferminator Incorporated, this brand stands for a whole new world order and will keep this status for a very long time. Until the next small seed will grow to tarnish.

Scenario II: Save our Nature (SON)

Save our nature (SON)

My name is Serafina Schwarzman Walters. I am 32 years old and a member of SON (Save our Nature). We care. We care for our lovely children who are our light and our precious, we care for humankind and we care for the world. Did you know that Ferminator Incorporated is the reason that millions of people lost their job due to their corrupt takeover and global establishment of total dependency (slavery) in the economy?
In the beginning of the 21 century, billions of dollars were invested in agricultural areas in overseas. This money was used to produce Biofuel.
Biological and sustainable products that were meant to replace those fossil fuels, that were tearing humanity apart for ages. The right approach towards the best goals. Imagine a world freed of the chains of oil companies, humankind living in peace and harmony, no reason to fight over resources. This is the world I want for my children. We were so close to achieve this. Then the devil incarnated appeared. Ferminator Incorporated, a company whose obvious goal is to prevent the world of coming to rest. They claim that they are fighting against landgrabbing, that what they do can actually help the world to become a better place. In my opinion they are either recklessly lying or have no respect for our world our nature and our life.

I agree that landgrabbing was an issue that caused a lot of problems for many people, but it ensured sustainable resources that mother nature granted us. Ferminator Incorporated uses genetic modified organisms (GMOs) for their biofuel production. There is a reason why GMO are strictly regulated by law and are widely doubted by society. Those cells are highly unpredictable and can be a serious threat to humanity. Imagine an outbreak of those cells, either accidently or on purpose. No one can stop them from going on a rampage against humanity. They are able to erase our kind of this planet. Just because of the merciless greed of Ferminator Incorporated.
Blasphemy aside, one can argue that Ferminator Incorporated developed methods for Biofuel production that could actually help to solve problems. Fermentation based production of Biofuel was suddenly efficient enough to replace conservative methods that required landgrabbing. Those agricultural areas, that were occupied by giant companies for plant based biofuel production, should have been giving back to the farmers that were working on it for ages until this land was stolen from them. That was a noble goal, I agree. But reality seems different. In fact, this land is still in the hands of big companies that grow plant resources that are used as a source for media that Ferminator Incorporated needs for his GMOs. Long story short, Ferminator Incorporated changed nothing. The world is still an unfair place for those who cannot fight for themselves. In contrast, Ferminator Incorporated established a Monopol, an economic Imperium. There is no more competition in market economy.

All there is, is Ferminator Incorporated forcing their products on us, dictating price and value of something our species depends on. Ferminator Incorporated is an Imperium and Steffen Lütke, its CEO, is the Dictator.
But remember, there were many empires. They rise, they shine and then they all fall. I demand that we as one stand up against the goliath that Ferminator Incorporated embodies. Even if they have money or political power, we are many and we have the duty as humans to stand against the oppressor of our....

...health

&

freedom!

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